

総括報告書

作成日:2024年3月11日

JCOG1109:「臨床病期 IB/Ⅱ/Ⅲ 食道癌(T4 を除く)に対する  
術前 CF 療法/術前 DCF 療法/術前 CF-RT 療法の第Ⅲ 相比較試験」

|               |         |                   |
|---------------|---------|-------------------|
| 研究代表者(研究代表医師) | 氏名 加藤 健 | 所属 国立がん研究センター中央病院 |
| 研究事務局         | 氏名 加藤健  | 所属 国立がん研究センター中央病院 |
| グループ代表者       | 氏名 竹内裕也 | 所属 浜松医科大学医学部      |

1 臨床研究の名称等

|                      |                                                                                                                                                                                                                 |
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| 実施計画の実施計画番号          | jRCTs031180202                                                                                                                                                                                                  |
| 研究名称                 | JCOG1109:臨床病期IB/Ⅱ/Ⅲ食道癌(T4を除く)に対する術前CF療法/術前DCF療法/術前CF-RT療法の第Ⅲ相比較試験<br>A randomized controlled phase Ⅲ trial comparing CF versus DCF versus CF-RT as neoadjuvant treatment for locally advanced esophageal cancer |
| 平易な研究名称              | JCOG1109:臨床病期IB/Ⅱ/Ⅲ食道癌(T4を除く)に対する術前療法の第Ⅲ相比較試験<br>RCT of Neoadjuvant therapy for Esophageal cancer by Triple arm NExT study                                                                                      |
| 認定臨床研究審査委員会の名称(認定番号) | 国立研究開発法人国立がん研究センター東病院臨床研究審査委員会(CRB3180009)                                                                                                                                                                      |

|      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
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| 試験概要 | <p><b>目的</b><br/>胸部食道癌 cStage IB/Ⅱ/Ⅲ(T4 を除く)患者を対象に、標準治療である術前 5-FU+CDDP(CF)療法に対する、3 剤併用術前化学療法(5-FU+CDDP+Docetaxel(DCF)療法)と、術前化学放射線療法(5-FU+CDDP+RT 41.4 Gy(CF-RT 療法))の優越性をランダム化第Ⅲ 相試験で検証する。</p> <p><b>対象</b></p> <ol style="list-style-type: none"><li>1) 組織学的に扁平上皮癌、腺扁平上皮癌、類基底細胞癌のいずれかと診断されている。</li><li>2) 食道病変がすべて胸部食道内(UICC-TNM 第7版)に局限する。</li><li>3) TNM分類(UICC-TNM 第7版)にて臨床病期cStage IB、ⅡまたはT4を除くⅢである。</li><li>4) 登録日の年齢が20歳以上、75歳以下である。</li><li>5) Performance status(PS)はECOGの規準で0または1である。</li><li>6) 測定可能病変の有無は問わない。</li><li>7) 食道癌に対する治療歴がない。</li><li>8) 他のがん種を含め、化学療法・放射線療法・内分泌療法の既往がない。</li><li>9) 登録前14日以内の最新の検査値で、臓器機能が保たれている。</li><li>10) 開胸手術(もしくは胸腔鏡下手術)および開腹手術(もしくは腹腔鏡下手術)による食道癌根治手術(R0)が可能と判断される。</li><li>11) 試験参加について患者本人から文書で同意が得られている。</li></ol> |
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**治療**

A 群:術前 CF 療法:5-FU+CDDP (800 mg/m<sup>2</sup>/day 1-5, 80 mg/m<sup>2</sup>/day 1, q3wks、2 コース)

| CF療法                          | 1        | 2 | 3 | 4        | 5 | 6 | 7 |
|-------------------------------|----------|---|---|----------|---|---|---|
|                               | WEEK     |   |   |          |   |   |   |
| CDDP (80mg/m <sup>2</sup> /d) | ↓        |   |   | ↓        |   |   |   |
| 5FU (800mg/m <sup>2</sup> /d) | □ Day1-5 |   |   | □ Day1-5 |   |   |   |

B 群:術前 DCF 療法:術前 DCF 療法:5-FU+CDDP+Docetaxel (750 mg/m<sup>2</sup>/day 1-5, 70 mg/m<sup>2</sup>/day 1, 70 mg/m<sup>2</sup>/day 1, q3wks、3 コース)

| DCF療法                             | 1        | 2 | 3 | 4        | 5 | 6 | 7        | 8 | 9 |
|-----------------------------------|----------|---|---|----------|---|---|----------|---|---|
|                                   | WEEK     |   |   |          |   |   |          |   |   |
| Docetaxel(70mg/m <sup>2</sup> /d) | ↓        |   |   | ↓        |   |   | ↓        |   |   |
| CDDP (70mg/m <sup>2</sup> /d)     | ↓        |   |   | ↓        |   |   | ↓        |   |   |
| 5FU (750mg/m <sup>2</sup> /d)     | □ Day1-5 |   |   | □ Day1-5 |   |   | □ Day1-5 |   |   |

C 群:術前 CF-RT 療法::5-FU+CDDP (1000 mg/m<sup>2</sup>/day 1-4, 75 mg/m<sup>2</sup>/day 1, q4wks、2 コース)+RT (41.4 Gy/23 fr/5w)

| CF-RT療法                              | 1        | 2 | 3 | 4 | 5        | 6 | 7 |
|--------------------------------------|----------|---|---|---|----------|---|---|
|                                      | WEEK     |   |   |   |          |   |   |
| CDDP (75mg/m <sup>2</sup> /d)        | ↓        |   |   |   | ↓        |   |   |
| 5FU (1000mg/m <sup>2</sup> /d)       | □ Day1-4 |   |   |   | □ Day1-4 |   |   |
| Radiation<br>(1.8Gy/fr x23 = 41.4Gy) | ■        | ■ | ■ | ■ | ■        |   |   |

手術療法(各群術前治療終了後に行う)

開胸手術(もしくは胸腔鏡下手術)および開腹手術(もしくは腹腔鏡下手術)による、2 領域以上のリンパ節郭清を伴う食道切除術

**エンドポイント**

Primary endpoint: 全生存期間

Secondary endpoint: 無増悪生存期間、根治切除割合、術前療法における奏効割合、病理組織学的完全奏効割合、術前療法中の有害事象発生割合、周術期合併症発生割合、晩期合併症発生割合、重篤な有害事象発生割合

**登録数・研究期間**

予定登録患者数:600 人(各群:200 人)、登録期間 6.25 年、追跡期間:登録終了後 5 年(主たる解析は登録終了後 3 年で行う)

## 2 臨床研究結果の要約

| 観察期間終了日                                                  | 2024年2月13日                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  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--------|---------|---------|----------|-------|---------|---------|
| Completion date                                          | 13 <sup>th</sup> February 2024                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              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  |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| 実施症例数                                                    | 601人                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        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   |         |         |          |       |         |         |
| Result actual enrolment                                  | 601                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         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   |         |         |          |       |         |         |
| 臨床研究の対象者の背景情報                                            | 全登録例 601 例を解析対象とした。年齢中央値は 65 歳(30–75 歳)、男性が 88%、PS 0 が 85%、食道扁平上皮癌が 98%、約 60%が胸部中部食道がん、Stage III が 62%であり、ほぼ事前に想定していた通りであった。各群の患者背景はバランスがとれていた。                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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   |         |         |          |       |         |         |
| Baseline Characteristics                                 | <table><tr><th>All patients</th><th>NeoCF (n=199)<br/>n (%)</th><th>NeoDCF (n=202)<br/>n (%)</th><th>NeoCF-RT (n=200)<br/>n (%)</th></tr><tr><td>Median age (range), years</td><td>65 (38–75)</td><td>64 (41–75)</td><td>65 (30–75)</td></tr><tr><td>Sex, n (%)</td><td></td><td></td><td></td></tr><tr><td>Male</td><td>178 (89.4)</td><td>178 (88.1)</td><td>173 (86.5)</td></tr><tr><td>Female</td><td>21 (10.6)</td><td>24 (11.9)</td><td>27 (13.5)</td></tr><tr><td>ECOG performance status, n (%)<sup>‡</sup></td><td></td><td></td><td></td></tr><tr><td>0</td><td>166 (83.4)</td><td>174 (86.1)</td><td>173 (86.5)</td></tr><tr><td>1</td><td>33 (16.6)</td><td>28 (13.9)</td><td>27 (13.5)</td></tr><tr><td>Histology at initial diagnosis, n (%)</td><td></td><td></td><td></td></tr><tr><td>Squamous cell carcinoma</td><td>197 (99.0)</td><td>198 (98.0)</td><td>196 (98.0)</td></tr><tr><td>Basal cell carcinoma</td><td>2 (1.0)</td><td>4 (2.0)</td><td>2 (1.0)</td></tr><tr><td>Adenosquamous cell carcinoma</td><td>0 (0)</td><td>0 (0)</td><td>2 (1.0)</td></tr><tr><td>Tumor location, n (%)</td><td></td><td></td><td></td></tr><tr><td>Upper</td><td>28 (14.1))</td><td>23 (11.4)</td><td>16 (8.0)</td></tr><tr><td>Middle</td><td>118 (59.3)</td><td>114 (56.4)</td><td>124 (62.0)</td></tr><tr><td>Lower</td><td>53 (26.6)</td><td>65 (32.2)</td><td>60 (30.0)</td></tr><tr><td>Clinical T stage, n (%)</td><td></td><td></td><td></td></tr><tr><td>cT1</td><td>24 (12.1)</td><td>19 (9.4)</td><td>22 (11.0)</td></tr><tr><td>cT2</td><td>38 (19.1)</td><td>45 (22.3)</td><td>42 (21.0)</td></tr><tr><td>cT3</td><td>137 (68.8)</td><td>138 (68.3)</td><td>136 (68.0)</td></tr><tr><td>Clinical N stage, n (%)</td><td></td><td></td><td></td></tr><tr><td>cN0</td><td>39 (19.6)</td><td>44 (21.8)</td><td>40 (20.0)</td></tr><tr><td>cN1</td><td>92 (46.2)</td><td>101 (50.0)</td><td>107 (53.5)</td></tr><tr><td>cN2</td><td>65 (32.7)</td><td>52 (25.7)</td><td>47 (23.5)</td></tr><tr><td>cN3</td><td>3 (1.5)</td><td>5 (2.5)</td><td>6 (3.0)</td></tr><tr><td>Clinical M stage, n (%)</td><td></td><td></td><td></td></tr><tr><td>cM0</td><td>199 (100.0)</td><td>201 (99.5)</td><td>198 (99.0)</td></tr><tr><td>cM1*</td><td>0 (0)</td><td>1 (0.5)</td><td>2 (1.0)</td></tr><tr><td>Clinical stage (UICC-TNM 7<sup>th</sup> edition), n (%)</td><td></td><td></td><td></td></tr><tr><td>Stage IB</td><td>14 (7.0)</td><td>19 (9.4)</td><td>19 (9.5)</td></tr><tr><td>Stage IIA</td><td>25 (12.6)</td><td>25 (12.4)</td><td>21 (10.5)</td></tr><tr><td>Stage IIB</td><td>38 (19.1)</td><td>32 (15.8)</td><td>35 (17.5)</td></tr><tr><td>Stage IIIA</td><td>64 (32.2)</td><td>81 (40.1)</td><td>82 (41.0)</td></tr><tr><td>Stage IIIB</td><td>55 (27.6)</td><td>39 (19.3)</td><td>35 (17.5)</td></tr><tr><td>Stage IIIC</td><td>3 (1.5)</td><td>5 (2.5)</td><td>6 (3.0)</td></tr><tr><td>Stage IV</td><td>0 (0)</td><td>1 (0.5)</td><td>2 (1.0)</td></tr></table> <p>*Supraclavicular lymph nodes were detected after enrollment. ECOG, Eastern Cooperative Oncology Group; NeoCF, neoadjuvant doublet chemotherapy consisting of 5-fluorouracil and cisplatin; NeoDCF, triplet chemotherapy consisting of 5-fluorouracil, cisplatin, and docetaxel; NeoCF+RT, doublet chemotherapy consisting of 5-fluorouracil and cisplatin with radiotherapy; TNM, Tumor–Node–Metastasis; UICC, International Union for Cancer Control</p> | All patients            | NeoCF (n=199)<br>n (%)    | NeoDCF (n=202)<br>n (%) | NeoCF-RT (n=200)<br>n (%) | Median age (range), years | 65 (38–75) | 64 (41–75) | 65 (30–75) | Sex, n (%) |  |  |  | Male | 178 (89.4) | 178 (88.1) | 173 (86.5) | Female | 21 (10.6) | 24 (11.9) | 27 (13.5) | ECOG performance status, n (%) <sup>‡</sup> |  |  |  | 0 | 166 (83.4) | 174 (86.1) | 173 (86.5) | 1 | 33 (16.6) | 28 (13.9) | 27 (13.5) | Histology at initial diagnosis, n (%) |  |  |  | Squamous cell carcinoma | 197 (99.0) | 198 (98.0) | 196 (98.0) | Basal cell carcinoma | 2 (1.0) | 4 (2.0) | 2 (1.0) | Adenosquamous cell carcinoma | 0 (0) | 0 (0) | 2 (1.0) | Tumor location, n (%) |  |  |  | Upper | 28 (14.1)) | 23 (11.4) | 16 (8.0) | Middle | 118 (59.3) | 114 (56.4) | 124 (62.0) | Lower | 53 (26.6) | 65 (32.2) | 60 (30.0) | Clinical T stage, n (%) |  |  |  | cT1 | 24 (12.1) | 19 (9.4) | 22 (11.0) | cT2 | 38 (19.1) | 45 (22.3) | 42 (21.0) | cT3 | 137 (68.8) | 138 (68.3) | 136 (68.0) | Clinical N stage, n (%) |  |  |  | cN0 | 39 (19.6) | 44 (21.8) | 40 (20.0) | cN1 | 92 (46.2) | 101 (50.0) | 107 (53.5) | cN2 | 65 (32.7) | 52 (25.7) | 47 (23.5) | cN3 | 3 (1.5) | 5 (2.5) | 6 (3.0) | Clinical M stage, n (%) |  |  |  | cM0 | 199 (100.0) | 201 (99.5) | 198 (99.0) | cM1* | 0 (0) | 1 (0.5) | 2 (1.0) | Clinical stage (UICC-TNM 7 <sup>th</sup> edition), n (%) |  |  |  | Stage IB | 14 (7.0) | 19 (9.4) | 19 (9.5) | Stage IIA | 25 (12.6) | 25 (12.4) | 21 (10.5) | Stage IIB | 38 (19.1) | 32 (15.8) | 35 (17.5) | Stage IIIA | 64 (32.2) | 81 (40.1) | 82 (41.0) | Stage IIIB | 55 (27.6) | 39 (19.3) | 35 (17.5) | Stage IIIC | 3 (1.5) | 5 (2.5) | 6 (3.0) | Stage IV | 0 (0) | 1 (0.5) | 2 (1.0) |
| All patients                                             | NeoCF (n=199)<br>n (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | NeoDCF (n=202)<br>n (%) | NeoCF-RT (n=200)<br>n (%) |                         |                           |                           |            |            |            |            |  |  |  |      |            |            |            |        |           |           |           |                                             |  |  |  |   |            |            |            |   |           |           |           |                                       |  |  |  |                         |            |            |            |                      |         |         |         |                              |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| Median age (range), years                                | 65 (38–75)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 64 (41–75)              | 65 (30–75)                |                         |                           |                           |            |            |            |            |  |  |  |      |            |            |            |        |           |           |           |                                             |  |  |  |   |            |            |            |   |           |           |           |                                       |  |  |  |                         |            |            |            |                      |         |         |         |                              |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| Sex, n (%)                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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  |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| Male                                                     | 178 (89.4)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  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  |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| Female                                                   | 21 (10.6)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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  |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| ECOG performance status, n (%) <sup>‡</sup>              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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  |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| 0                                                        | 166 (83.4)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  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  |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| 1                                                        | 33 (16.6)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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  |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| Histology at initial diagnosis, n (%)                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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   |         |         |          |       |         |         |
| Squamous cell carcinoma                                  | 197 (99.0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 198 (98.0)              | 196 (98.0)                |                         |                           |                           |            |            |            |            |  |  |  |      |            |            |            |        |           |           |           |                                             |  |  |  |   |            |            |            |   |           |           |           |                                       |  |  |  |                         |            |            |            |                      |         |         |         |                              |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| Basal cell carcinoma                                     | 2 (1.0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 4 (2.0)                 | 2 (1.0)                   |                         |                           |                           |            |            |            |            |  |  |  |      |            |            |            |        |           |           |           |                                             |  |  |  |   |            |            |            |   |           |           |           |                                       |  |  |  |                         |            |            |            |                      |         |         |         |                              |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| Adenosquamous cell carcinoma                             | 0 (0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 0 (0)                   | 2 (1.0)                   |                         |                           |                           |            |            |            |            |  |  |  |      |            |            |            |        |           |           |           |                                             |  |  |  |   |            |            |            |   |           |           |           |                                       |  |  |  |                         |            |            |            |                      |         |         |         |                              |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| Tumor location, n (%)                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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  |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| Upper                                                    | 28 (14.1))                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  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  |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| Middle                                                   | 118 (59.3)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  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  |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| Lower                                                    | 53 (26.6)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 65 (32.2)               | 60 (30.0)                 |                         |                           |                           |            |            |            |            |  |  |  |      |            |            |            |        |           |           |           |                                             |  |  |  |   |            |            |            |   |           |           |           |                                       |  |  |  |                         |            |            |            |                      |         |         |         |                              |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| Clinical T stage, n (%)                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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  |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| cT1                                                      | 24 (12.1)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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  |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| cT2                                                      | 38 (19.1)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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  |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| cT3                                                      | 137 (68.8)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  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  |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| Clinical N stage, n (%)                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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  |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| cN0                                                      | 39 (19.6)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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  |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| cN1                                                      | 92 (46.2)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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  |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| cN2                                                      | 65 (32.7)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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  |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| cN3                                                      | 3 (1.5)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     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  |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| Clinical M stage, n (%)                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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   |         |         |          |       |         |         |
| cM0                                                      | 199 (100.0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 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  |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| cM1*                                                     | 0 (0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 1 (0.5)                 | 2 (1.0)                   |                         |                           |                           |            |            |            |            |  |  |  |      |            |            |            |        |           |           |           |                                             |  |  |  |   |            |            |            |   |           |           |           |                                       |  |  |  |                         |            |            |            |                      |         |         |         |                              |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| Clinical stage (UICC-TNM 7 <sup>th</sup> edition), n (%) |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             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   |         |         |          |       |         |         |
| Stage IB                                                 | 14 (7.0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    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  |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| Stage IIA                                                | 25 (12.6)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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  |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| Stage IIB                                                | 38 (19.1)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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   |         |         |          |       |         |         |
| Stage IIIA                                               | 64 (32.2)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 81 (40.1)               | 82 (41.0)                 |                         |                           |                           |            |            |            |            |  |  |  |      |            |            |            |        |           |           |           |                                             |  |  |  |   |            |            |            |   |           |           |           |                                       |  |  |  |                         |            |            |            |                      |         |         |         |                            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   |         |         |          |       |         |         |
| Stage IIIB                                               | 55 (27.6)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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  |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| Stage IIIC                                               | 3 (1.5)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 5 (2.5)                 | 6 (3.0)                   |                         |                           |                           |            |            |            |            |  |  |  |      |            |            |            |        |           |           |           |                                             |  |  |  |   |            |            |            |   |           |           |           |                                       |  |  |  |                         |            |            |            |                      |         |         |         |                              |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| Stage IV                                                 | 0 (0)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | 1 (0.5)                 | 2 (1.0)                   |                         |                           |                           |            |            |            |            |  |  |  |      |            |            |            |        |           |           |           |                                             |  |  |  |   |            |            |            |   |           |           |           |                                       |  |  |  |                         |            |            |            |                      |         |         |         |                              |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |
| 臨床研究のデザインに応じた進行状況に関する情報                                  | 2012年12月5日に登録開始した。登録ペースは、当初予測したペースを上回るペースであったため、2015年6月8日に行われた第3回改訂にて、予定登録数を当初の501人から600人へ増やす改訂を行った。これにより、検出力70%が80%へと増加した。その後も予定登録ペースを上回る患者登録が継続された。B群とC群が、ともにA群に対する優越性を示した場合、B群とC群のみで登録を継続する予定であったため、すべての患者の登録が終了する半年前の定期モニタリングに合わせて、2018年3月17日に第2回中間解析が行われたが、効果・安全性評価委員会からは、「研究の継続を認める」とのコメントであった。最終的に2018年7月20日に登録が終了し、2021年11月19                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                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  |       |       |         |                       |  |  |  |       |            |           |          |        |            |            |            |       |           |           |           |                         |  |  |  |     |           |          |           |     |           |           |           |     |            |            |            |                         |  |  |  |     |           |           |           |     |           |            |            |     |           |           |           |     |         |         |         |                         |  |  |  |     |             |            |            |      |       |         |         |                                                          |  |  |  |          |          |          |          |           |           |           |           |           |           |           |           |            |           |           |           |            |           |           |           |            |         |         |         |          |       |         |         |

日に提出された主たる解析レポートにおいて、術前DCF療法が術前CF療法に比して有意に生存期間が良好であったことが示された。

38施設から1人以上の患者登録があり、登録がなかったのは7施設であった。国立がん研究センター中央病院が90人(15.0%)と最も患者登録数が多く、次いで東海大学医学部(61人)、神奈川県立がんセンター(36人)であった。

プロトコルで規定した術前化学療法は、601人中580人で行われ、546人で手術が行われた。

Participant flow

Figure 1. CONSORT Diagram

Enrollment

Enrolled and randomly assigned  
(n = 601)

Assigned to NeoCF arm (intention-to-treat population)  
(n=193)  
Synchronous malignancy (n=3)  
R0 resection not expected (n=1)  
Concomitant disease (n=2)

Assigned to NeoDCF arm (intention-to-treat population)  
(n=203)  
Disease progression before neoadjuvant treatment (n=1)  
Synchronous malignancy (n=2)  
Ineligible disease (n=1)  
Concomitant disease (n=2)

Assigned to NeoCF-RT arm (intention-to-treat population)  
(n=200)  
Disease progression before neoadjuvant treatment (n=2)  
Synchronous malignancy (n=1)  
Ineligible disease (n=2)  
Withdrew consent before neoadjuvant treatment (n=4)

Eligible patients (n=193)

Eligible patients (n=199)

Eligible patients (n=197)

Received neoadjuvant treatment (safety analysis population) (n=193)  
No surgery (n=8)  
Disease progression (n=6)  
Patient refusal (n=2)

Received neoadjuvant treatment (safety analysis population) (n=196)  
No surgery (n=13)  
Disease progression (n=6)  
Patient refusal (n=8)  
No recovery of toxicity to within the limit (n=1)  
Death during neoadjuvant therapy (n=1)

Received neoadjuvant treatment (safety analysis population) (n = 191)  
No surgery (n=13)  
Disease progression (n=5)  
No recovery of toxicity to within the limit (n=4)  
Patient refusal (n=3)  
Other disease (n=1)

Patients who underwent surgery (surgical outcomes analysis population) (n = 185)

Patients who underwent surgery (surgical outcomes analysis population) (n=183)

Patients who underwent surgery (surgical outcomes analysis population) (n=178)

疾病等の発生状況のまとめ

術前治療における安全性解析は、NeoCF 群で 193 人、NeoDCF 群で 196 人、NeoCF-RT 群で 191 人の患者について実施された。Grade 3/4 の好中球減少症と発熱性好中球減少症は、NeoCF 群(24.0%と 1.0%)や NeoCF-RT 群(44.5%と 5.2%)よりも、NeoDCF 群(85.2%と 17.3%)でより多く発生した。食道炎は NeoCF 群(2.6%)や NeoDCF 群(4.6%)よりも NeoCF-RT 群(60.7%)でより発生した。術前治療中止に関連した有害事象は、NeoDCF 群で他の群(NeoCF-RT 群および NeoCF 群)よりも多く認められた(8.9%、6.0%および 4.0%)。術前治療における治療関連死亡割合は低く、群間で差を認めなかった(NeoCF 群 4 人(2.0%)、NeoDCF 群 4 人(2.0%)、NeoCF-RT 群 4 人(2.0%))。

術後合併症(Grade $\geq$ 2)の頻度は、治療群間で同程度であった。肺炎、吻合部漏出、反回神経麻痺の割合はそれぞれ、NeoCF 群10.3%、10.3%、15.1%、NeoDCF 群9.8%、8.7%、10.4%、NeoCF-RT 群12.9%、12.9%、9.6%であった。術後在院死亡は、30日以内で3人(NeoCF 群で2人、NeoCF-RT 群で1人)、60日以内はNeoDCF 群で1人、それ以上で2人(NeoCF 群とNeoDCF 群で各1人)であった。再手術および入院患者の死亡割合は、すべての治療群で5%未満であった。

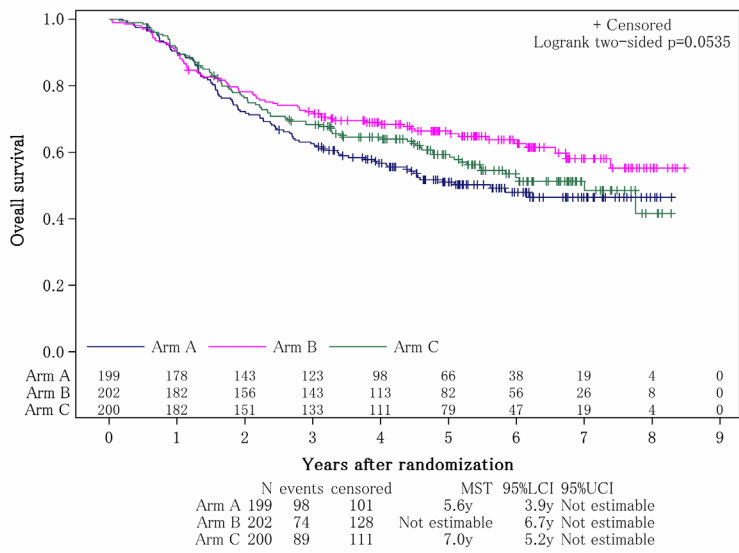
Adverse events

(A) Adverse events during neoadjuvant therapy

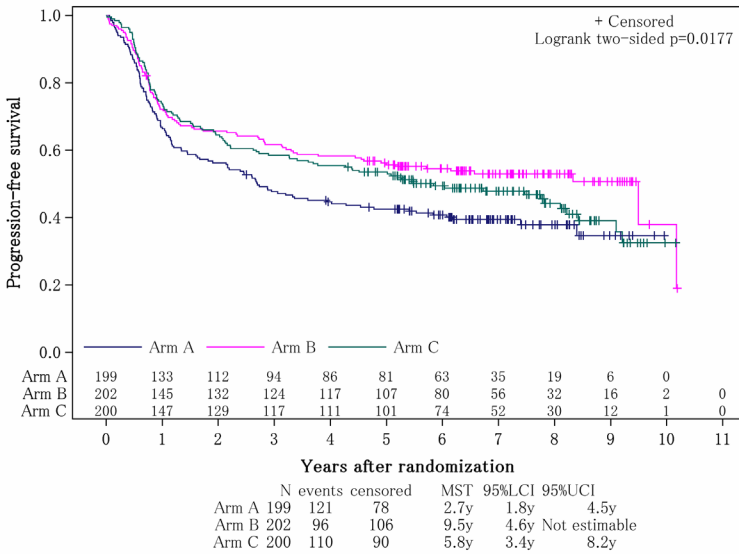
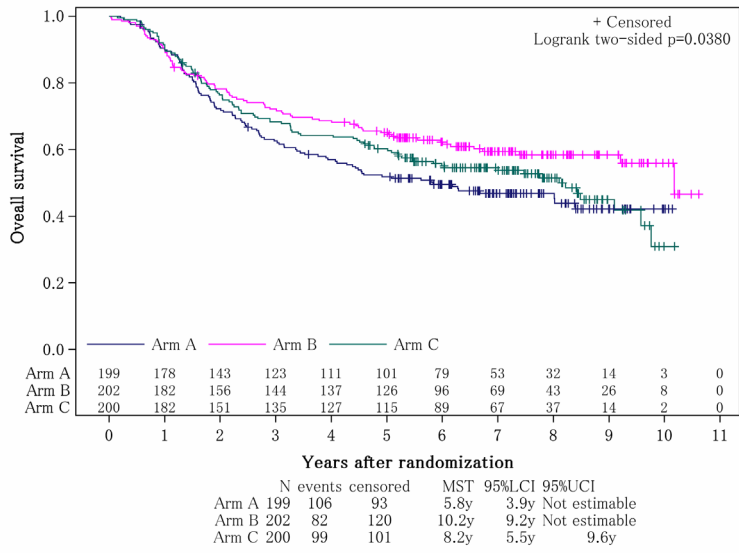
|                                                                                      | NeoCF (n=193)*     |                    | NeoCF+D (n=196)*   |                    | NeoCF+RT (n=191)*  |                    |
|--------------------------------------------------------------------------------------|--------------------|--------------------|--------------------|--------------------|--------------------|--------------------|
|                                                                                      | Any grade<br>n (%) | Grade 3/4<br>n (%) | Any grade<br>n (%) | Grade 3/4<br>n (%) | Any grade<br>n (%) | Grade 3/4<br>n (%) |
| Adverse events related to treatment in $\geq 10\%$ of patients in any treatment arm† |                    |                    |                    |                    |                    |                    |
| Leukocytopenia                                                                       | 83 (43.0)          | 13 (6.7)           | 182 (92.9)         | 126 (64.3)         | 180 (94.2)         | 103 (53.9)         |
| Thrombocytopenia                                                                     | 106 (54.9)         | 4 (2.1)            | 122 (62.2)         | 2 (1.0)            | 169 (88.5)         | 12 (6.3)           |
| Neutropenia                                                                          | 136 (70.8)         | 46 (24.0)          | 192 (98.0)         | 167 (85.2)         | 173 (90.6)         | 85 (44.5)          |
| Elevated AST                                                                         | 64 (33.2)          | 0 (0.0)            | 94 (48.0)          | 6 (3.1)            | 66 (34.6)          | 1 (0.5)            |
| Elevated ALT                                                                         | 74 (38.3)          | 2 (1.0)            | 90 (45.9)          | 6 (3.1)            | 63 (33.0)          | 2 (1.1)            |
| Elevated creatinine                                                                  | 67 (34.7)          | 4 (2.1)            | 70 (35.7)          | 1 (0.5)            | 57 (29.8)          | 1 (0.5)            |
| Hyponatremia                                                                         | 155 (80.3)         | 13 (6.7)           | 175 (89.3)         | 51 (26.0)          | 159 (83.2)         | 21 (11.0)          |
| Stomatitis                                                                           | 65 (33.7)          | 2 (1.0)            | 90 (45.9)          | 11 (5.6)           | 46 (24.1)          | 2 (1.0)            |
| Esophagitis                                                                          | 5 (2.6)            | 2 (1.0)            | 9 (4.6)            | 2 (1.0)            | 116 (60.7)         | 17 (8.9)           |
| Febrile neutropenia                                                                  | 2 (1.0)            | 2 (1.0)            | 34 (17.3)          | 34 (17.3)          | 10 (5.2)           | 10 (5.2)           |
| Loss of appetite                                                                     | 125 (64.8)         | 16 (8.3)           | 152 (77.6)         | 42 (21.4)          | 127 (66.5)         | 28 (14.7)          |
| Dysphagia                                                                            | 34 (17.6)          | 11 (5.7)           | 23 (11.7)          | 4 (2.0)            | 50 (26.2)          | 9 (4.7)            |

\*Patients who received at least one course of chemotherapy. AST, aspartate transaminase; ALT, alanine transaminase;

|                                     | <p>NeoCF, neoadjuvant doublet chemotherapy consisting of 5-fluorouracil and cisplatin; NeoDCF, triplet chemotherapy consisting of 5-fluorouracil, cisplatin, and docetaxel; NeoCF+RT, doublet chemotherapy consisting of 5-fluorouracil and cisplatin with radiotherapy</p> <p>(B) Surgical complications</p> <table><tr><th></th><th colspan="2">NeoCF (n=185)</th><th colspan="2">NeoCF+D (n=183)</th><th colspan="2">NeoCF+RT (n=178)</th></tr><tr><th></th><th>Any grade n (%)</th><th>Grade 2–4 n (%)</th><th>Any grade n (%)</th><th>Grade 2–4 n (%)</th><th>Any grade n (%)</th><th>Grade 2–4 n (%)</th></tr><tr><td>Pneumonia</td><td>19 (10.3)</td><td>19 (10.3)</td><td>18 (9.8)</td><td>18 (9.8)</td><td>23 (12.9)</td><td>23 (12.9)</td></tr><tr><td>Anastomotic leakage</td><td>21 (11.4)</td><td>19 (10.3)</td><td>17 (9.3)</td><td>16 (8.7)</td><td>24 (13.5)</td><td>23 (12.9)</td></tr><tr><td>Recurrent laryngeal nerve paralysis</td><td>51 (27.6)</td><td>28 (15.1)</td><td>39 (21.3)</td><td>19 (10.4)</td><td>43 (24.2)</td><td>17 (9.6)</td></tr><tr><td>Chylothorax</td><td>4 (2.2)</td><td>2 (1.1)</td><td>10 (5.5)</td><td>7 (3.8)</td><td>12 (6.7)</td><td>9 (5.1)</td></tr><tr><td>Wound infection</td><td>15 (8.1)</td><td>15 (8.1)</td><td>11 (6.0)</td><td>11 (6.0)</td><td>14 (7.9)</td><td>14 (7.9)</td></tr><tr><td>Pleural effusion</td><td>35 (18.9)</td><td>22 (11.9)</td><td>29 (15.8)</td><td>20 (10.9)</td><td>36 (20.2)</td><td>25 (14.0)</td></tr><tr><td>Re-operation</td><td colspan="2">5 (2.7)</td><td colspan="2">6 (3.3)</td><td colspan="2">7 (3.9)</td></tr><tr><td>In-hospital death</td><td colspan="2">3 (1.6)</td><td colspan="2">2 (1.1)</td><td colspan="2">1 (0.6)</td></tr></table> <p><b>**Patients who received at least one course of chemotherapy and underwent surgery. NeoCF, neoadjuvant doublet chemotherapy consisting of 5-fluorouracil and cisplatin; NeoDCF, triplet chemotherapy consisting of 5-fluorouracil, cisplatin, and docetaxel; NeoCF+RT, doublet chemotherapy consisting of 5-fluorouracil and cisplatin with radiotherapy</b></p> |                 | NeoCF (n=185)   |                 | NeoCF+D (n=183)  |                 | NeoCF+RT (n=178) |  |  | Any grade n (%) | Grade 2–4 n (%) | Any grade n (%) | Grade 2–4 n (%) | Any grade n (%) | Grade 2–4 n (%) | Pneumonia | 19 (10.3) | 19 (10.3) | 18 (9.8) | 18 (9.8) | 23 (12.9) | 23 (12.9) | Anastomotic leakage | 21 (11.4) | 19 (10.3) | 17 (9.3) | 16 (8.7) | 24 (13.5) | 23 (12.9) | Recurrent laryngeal nerve paralysis | 51 (27.6) | 28 (15.1) | 39 (21.3) | 19 (10.4) | 43 (24.2) | 17 (9.6) | Chylothorax | 4 (2.2) | 2 (1.1) | 10 (5.5) | 7 (3.8) | 12 (6.7) | 9 (5.1) | Wound infection | 15 (8.1) | 15 (8.1) | 11 (6.0) | 11 (6.0) | 14 (7.9) | 14 (7.9) | Pleural effusion | 35 (18.9) | 22 (11.9) | 29 (15.8) | 20 (10.9) | 36 (20.2) | 25 (14.0) | Re-operation | 5 (2.7) |  | 6 (3.3) |  | 7 (3.9) |  | In-hospital death | 3 (1.6) |  | 2 (1.1) |  | 1 (0.6) |  |
|-------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------|-----------------|-----------------|------------------|-----------------|------------------|--|--|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------|-----------|-----------|----------|----------|-----------|-----------|---------------------|-----------|-----------|----------|----------|-----------|-----------|-------------------------------------|-----------|-----------|-----------|-----------|-----------|----------|-------------|---------|---------|----------|---------|----------|---------|-----------------|----------|----------|----------|----------|----------|----------|------------------|-----------|-----------|-----------|-----------|-----------|-----------|--------------|---------|--|---------|--|---------|--|-------------------|---------|--|---------|--|---------|--|
|                                     | NeoCF (n=185)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                 | NeoCF+D (n=183) |                 | NeoCF+RT (n=178) |                 |                  |  |  |                 |                 |                 |                 |                 |                 |           |           |           |          |          |           |           |                     |           |           |          |          |           |           |                                     |           |           |           |           |           |          |             |         |         |          |         |          |         |                 |          |          |          |          |          |          |                  |           |           |           |           |           |           |              |         |  |         |  |         |  |                   |         |  |         |  |         |  |
|                                     | Any grade n (%)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Grade 2–4 n (%) | Any grade n (%) | Grade 2–4 n (%) | Any grade n (%)  | Grade 2–4 n (%) |                  |  |  |                 |                 |                 |                 |                 |                 |           |           |           |          |          |           |           |                     |           |           |          |          |           |           |                                     |           |           |           |           |           |          |             |         |         |          |         |          |         |                 |          |          |          |          |          |          |                  |           |           |           |           |           |           |              |         |  |         |  |         |  |                   |         |  |         |  |         |  |
| Pneumonia                           | 19 (10.3)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 19 (10.3)       | 18 (9.8)        | 18 (9.8)        | 23 (12.9)        | 23 (12.9)       |                  |  |  |                 |                 |                 |                 |                 |                 |           |           |           |          |          |           |           |                     |           |           |          |          |           |           |                                     |           |           |           |           |           |          |             |         |         |          |         |          |         |                 |          |          |          |          |          |          |                  |           |           |           |           |           |           |              |         |  |         |  |         |  |                   |         |  |         |  |         |  |
| Anastomotic leakage                 | 21 (11.4)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 19 (10.3)       | 17 (9.3)        | 16 (8.7)        | 24 (13.5)        | 23 (12.9)       |                  |  |  |                 |                 |                 |                 |                 |                 |           |           |           |          |          |           |           |                     |           |           |          |          |           |           |                                     |           |           |           |           |           |          |             |         |         |          |         |          |         |                 |          |          |          |          |          |          |                  |           |           |           |           |           |           |              |         |  |         |  |         |  |                   |         |  |         |  |         |  |
| Recurrent laryngeal nerve paralysis | 51 (27.6)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 28 (15.1)       | 39 (21.3)       | 19 (10.4)       | 43 (24.2)        | 17 (9.6)        |                  |  |  |                 |                 |                 |                 |                 |                 |           |           |           |          |          |           |           |                     |           |           |          |          |           |           |                                     |           |           |           |           |           |          |             |         |         |          |         |          |         |                 |          |          |          |          |          |          |                  |           |           |           |           |           |           |              |         |  |         |  |         |  |                   |         |  |         |  |         |  |
| Chylothorax                         | 4 (2.2)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | 2 (1.1)         | 10 (5.5)        | 7 (3.8)         | 12 (6.7)         | 9 (5.1)         |                  |  |  |                 |                 |                 |                 |                 |                 |           |           |           |          |          |           |           |                     |           |           |          |          |           |           |                                     |           |           |           |           |           |          |             |         |         |          |         |          |         |                 |          |          |          |          |          |          |                  |           |           |           |           |           |           |              |         |  |         |  |         |  |                   |         |  |         |  |         |  |
| Wound infection                     | 15 (8.1)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            | 15 (8.1)        | 11 (6.0)        | 11 (6.0)        | 14 (7.9)         | 14 (7.9)        |                  |  |  |                 |                 |                 |                 |                 |                 |           |           |           |          |          |           |           |                     |           |           |          |          |           |           |                                     |           |           |           |           |           |          |             |         |         |          |         |          |         |                 |          |          |          |          |          |          |                  |           |           |           |           |           |           |              |         |  |         |  |         |  |                   |         |  |         |  |         |  |
| Pleural effusion                    | 35 (18.9)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           | 22 (11.9)       | 29 (15.8)       | 20 (10.9)       | 36 (20.2)        | 25 (14.0)       |                  |  |  |                 |                 |                 |                 |                 |                 |           |           |           |          |          |           |           |                     |           |           |          |          |           |           |                                     |           |           |           |           |           |          |             |         |         |          |         |          |         |                 |          |          |          |          |          |          |                  |           |           |           |           |           |           |              |         |  |         |  |         |  |                   |         |  |         |  |         |  |
| Re-operation                        | 5 (2.7)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                 | 6 (3.3)         |                 | 7 (3.9)          |                 |                  |  |  |                 |                 |                 |                 |                 |                 |           |           |           |          |          |           |           |                     |           |           |          |          |           |           |                                     |           |           |           |           |           |          |             |         |         |          |         |          |         |                 |          |          |          |          |          |          |                  |           |           |           |           |           |           |              |         |  |         |  |         |  |                   |         |  |         |  |         |  |
| In-hospital death                   | 3 (1.6)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                 | 2 (1.1)         |                 | 1 (0.6)          |                 |                  |  |  |                 |                 |                 |                 |                 |                 |           |           |           |          |          |           |           |                     |           |           |          |          |           |           |                                     |           |           |           |           |           |          |             |         |         |          |         |          |         |                 |          |          |          |          |          |          |                  |           |           |           |           |           |           |              |         |  |         |  |         |  |                   |         |  |         |  |         |  |
| 主要評価項目及び副次評価項目のデータ解析及び結果            | <p>本試験ではprimary endpointを全生存期間とし、標準治療であるNeoCF群に対して、試験治療であるNeoDCF群、NeoCF-RT群それぞれが優るかどうかを検証した。</p> <p>主たる解析時点（追跡調査2021年7月20日）において、3年生存割合はNeoCF群：62.6%、NeoDCF群：72.1%、NeoCF-RT群：68.3%であり、層別Cox回帰に基づくNeoDCF群のNeoCF群に対するHRは0.68(95% CI 0.50–0.92)、NeoCF-RT群のNeoCF群に対するHRIは0.84(95% CI 0.63–1.12)であった。層別ログランク検定による片側p値が多重性を調整した有意水準を下回ったため、NeoDCF群ではNeoCF群に対する優越性が示された(p値0.0055&lt;0.0248)が、NeoCF-RT群では統計学的有意差は見られなかった(p値0.12)。</p> <p>最終解析時点（追跡調査2023年7月20日）においては、5年生存割合はNeoCF群：51.9%、NeoDCF群：65.1%、NeoCF-RT群：60.2%であり、層別Cox回帰に基づくNeoDCF群のNeoCF群に対するHRは0.68(95% CI 0.51–0.91)、NeoCF-RT群のNeoCF群に対するHRIは0.86(95% CI 0.66–1.14)であった。Secondary endpointである無増悪生存期間については、5年無増悪生存割合はNeoCF群：42.6%、NeoDCF群：55.7%、NeoCF-RT群：53.5%であり、NeoDCF群で良好な傾向を認めた（NeoDCF群のNeoCF群に対するHR 0.69, 95% CI 0.53–0.90）。増悪例はNeoCF群：104例、NeoDCF群：82例、NeoCF-RT群79例であり、そのうち局所増悪のみは38例(36.5%)、36例(43.9%)、18例(22.8%)、遠隔転移を含む増悪は66例(63.5%)、46例(56.1%)、61例(77.2%)であり、NeoCF-RT群では局所増悪のみの患者が少なく、遠隔転移を含む増悪例が多い傾向であった。</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                 |                 |                 |                  |                 |                  |  |  |                 |                 |                 |                 |                 |                 |           |           |           |          |          |           |           |                     |           |           |          |          |           |           |                                     |           |           |           |           |           |          |             |         |         |          |         |          |         |                 |          |          |          |          |          |          |                  |           |           |           |           |           |           |              |         |  |         |  |         |  |                   |         |  |         |  |         |  |
| Outcome measures                    | <p><b>Primary analysis using data as of July 20, 2021</b></p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |                 |                 |                 |                  |                 |                  |  |  |                 |                 |                 |                 |                 |                 |           |           |           |          |          |           |           |                     |           |           |          |          |           |           |                                     |           |           |           |           |           |          |             |         |         |          |         |          |         |                 |          |          |          |          |          |          |                  |           |           |           |           |           |           |              |         |  |         |  |         |  |                   |         |  |         |  |         |  |



Final analysis using data as of July 20, 2023



|                                                      | Site of recurrence                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | NeoCF (n=104)<br>n (%) | NeoCF+D (n=82)<br>n (%) | NeoCF+RT (n=79)<br>n (%) |
|------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|-------------------------|--------------------------|
|                                                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                        |                         |                          |
|                                                      | Locoregional only                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | 38 (36.5)              | 36 (43.9)               | 18 (22.8)                |
|                                                      | Any distant                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 66 (63.5)              | 46 (56.1)               | 61 (77.2)                |
|                                                      | Distant and locoregional                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 26 (25.0)              | 19 (23.2)               | 22 (27.8)                |
|                                                      | Distant only                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 40 (38.5)              | 27 (32.9)               | 39 (49.4)                |
| 簡潔な要約                                                | <p>局所進行切除可能食道扁平上皮がん(臨床病期IB,IIまたはT4を除くⅢ(UICC-TNM7版))に対して、術前DCF療法は、標準治療であった術前CF療法に比して有意差をもって生存期間を延長し、新たな標準治療であると考えられた。周術期合併症は術前CF療法と術前DCF療法で同等であった。術前治療による合併症については、血液毒性や、消化器毒性、発熱性好中球減少の割合は術前DCF療法で増加したが許容範囲と考えられた。一方で、欧米などでの標準治療の一つである術前CF-RT療法は、術前CF療法に比して、有意な生存期間の延長効果を示せなかった。その理由として、術前CF-RT療法において、遠隔転移再発が術前DCF療法と比べて多いこと、がん以外の疾病による死亡が多かったことなどが考えられた。</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                        |                         |                          |
| Brief summary                                        | <p>In patients with locally advanced resectable esophageal squamous cell carcinoma (clinical stage IB, II, or III excluding T4 according to UICC-TNM 7th edition), neoadjuvant DCF therapy was considered to be a new standard treatment as it significantly prolonged survival compared to the former standard neoadjuvant CF therapy. Perioperative complications were considered comparable, but an increase in hematologic toxicity, gastrointestinal toxicity, and the proportion of febrile neutropenia was observed more in neoadjuvant DCF therapy during preoperative treatment, although it was considered within the acceptable range. On the other hand, neoadjuvant CF-RT therapy, which is one of the standard treatments in Western countries, did not show a significant survival benefit compared to neoadjuvant CF therapy. The reasons for this could be the higher proportion of distant metastasis recurrence and more deaths due to non-cancerous diseases in the neoadjuvant CF-RT therapy compared to neoadjuvant DCF therapy.</p> |                        |                         |                          |
| 公開予定日                                                | 2024年6月5日                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                        |                         |                          |
| 結果に関する最初の出版物での発表日                                    |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                        |                         |                          |
| Date of the first journal publication of results     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                        |                         |                          |
| 結果と出版物に関するURL (複数可)                                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                        |                         |                          |
| URL hyperlink(s) related to results and publications |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |                        |                         |                          |

### 3 IPD (individual clinical trial participant-level data) シェアリング (匿名化された臨床研究の対象者単位のデータの共有)

|                   |                                                                                                                                                                                                   |
|-------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| IPDデータを共有する計画     | ■あり    □なし    □未定                                                                                                                                                                                 |
| Plan to share IPD | Present                                                                                                                                                                                           |
| 計画の説明             | <p>① JCOG試験のデータシェアリングを行う場合、原則としてJCOG研究者との共同研究とし、最終的なデータ提供の可否はグループ代表者が決定する</p> <p>② 主たる解析結果の論文公表後とする</p> <p>③ データを提供した事実をJCOGウェブサイト公開する</p> <p>④ 共同研究者は、解析プログラム、ログ、アウトプットの3点をJCOGデータセンターへ送付する。</p> |

|                  |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Plan description | <p>Individual participant data that underlie the results reported in this article, after deidentification will be shared if investigators whose proposed use of the data has been approved by the investigators from Japan Esophageal Oncology Group identified for this purpose. Proposals should be directed to <a href="mailto:kenkato@ncc.go.jp">kenkato@ncc.go.jp</a> and plans will be done according to following procedure.</p> <ol style="list-style-type: none"><li>① When sharing data from the JCOG study, in principle it will be collaborative research with JCOG researchers, and the final decision to provide data will be made by the group chair.</li><li>② It should be done after publication of the main analysis results</li><li>③ Publish the fact that the data was provided on the JCOG website</li><li>④ The collaborative researchers should provide the analysis program, logs, and output to the JCOG Data Center.</li></ol> |
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